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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,137	10/06/2006	Andrew Douglas Baxter	GJE-7705	7780

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SALIWANCHIK LLOYD & SALIWANCHIK
A PROFESSIONAL ASSOCIATION
PO Box 142950
GAINESVILLE, FL 32614

EXAMINER	
GUDIBANDE, SATYANARAYAN R	
ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
04/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,137	BAXTER ET AL.	
	Examiner	Art Unit	
	SATYANARAYANA R. GUDIBANDE	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *29 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,16 and 18* is/are pending in the application.

4a) Of the above claim(s) *3-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 16 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendments/Arguments

Claims 1 and 16 have been amended so that claim 1 corresponds to the elected group.

Claims 1-14, 16 and 18 are pending. Claims 15 and 17 have been canceled. Claims 3-14 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/13/08.

Claims 1, 2, 16 and 18 are examined on the merit.

Applicant's amendment to claims in the response filed on 12/19/08 has been acknowledged.

Any objections and/or rejections made in the office action dated 6/25/08 and not specifically discussed below in original or modified form are considered withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 16 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection has been modified to reflect the amendments made to claim 16. Response to applicant's argument appears at the end of the reiterated rejection.

The claim recite a limitation "compound in the form of the enantiomer or diastereomer that has little or no activity at an α or β-adrenoceptor". The claim as recited as the term "α or β adrenoceptor" lacks antecedent basis in the base claim.

Response to Arguments

Applicants state that applicant's have amended the claim 16 to address the issue identified by the office.

Applicant's arguments filed 12/29/08 have been fully considered but they are not persuasive. The issue was the lack of antecedent basis for the limitation recited in the claim, i.e., "compound in the form of the enantiomer or diastereomer that has little or no activity at an α or β adrenoceptor". This claim limitation does not appear in the base claim 1 from which the claim 16 depends from.

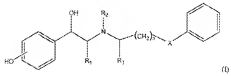
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

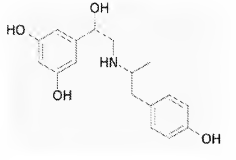
1. Claims 1 and 18 remain rejected under 35 U.S.C. 102(b) as being anticipated by Holen, APMIS, 1998, pages 849-857, Vol. 106 as stated in the office action dated 6/25/08. The rejection has been modified to reflect the amendments made to the claim 1 and addition of new claim 18. Response to applicant's argument appears at the end of the reiterated rejection.

In the instant invention, applicants claim a method for the treatment of a condition associated with T-cell proliferation or that is mediated by pro- and/or anti-inflammatory cytokines by administering a compound of formula I:



wherein the compound is selected from bufeniode, denopamine, ifenprodil, isoxsuprine, labetalol, medroxalol, mesuprine, nylidrin, protokylol, ractopamine, ritodrine, salmefamol and sulfinatol.

The compound taught by Holen has the following structure,



that reads on the formula I of instant claims 1 and 18 as follows:

Instant claims 1 and 18	Compound of Holen
R_1 = H or Me	R_1 = H
R_2 = H or alkyl	R_2 = H
R_3 = H or Me	R_3 = Me
n = 0 or 2	n = 0
X = CH_2 or O	X = CH_2

The reference also reaches that administration of fenoterol to patients was performed to study the effect of the drug on T-cell proliferation. The results indicated that administration of compound of Holen a β2-adrenoceptor agonist influenced T-cell growth and function (abstract). The reference also discloses that β2-adrenoceptor agonists are widely used in treatment of asthma which is a chronic disorder of airway inflammation (page 849, paragraphs 1 and 2). This meets the limitations of claims 1 and 18. Hence Holen anticipates instant invention.

Response to Arguments

Applicants argue that claim 1 has been amended to remove the reference to fenoterol and hence Holen does not anticipate the instant invention.

Applicant's arguments filed 12/19/08 have been fully considered but they are not persuasive. By removing a name from a list compounds recited in the claim does not overcome the rejection of a claim that is drawn to a structure of formula I. The compound taught in Holen continues to anticipates the compounds of formula I of instant invention recited in claims 1 and 18 as shown in the modified rejection above. In order for the compound fenoterol of Holen not to anticipate the instant claim, the compound of formula should be amended to so that the formula I does not correspond to fenoterol. By just amending the claim not to recite the name of a compound encompassed by the general formula does not remove the anticipation rejection that continues to read on the chemical formula of the named species.

2. Claims 1 and 18 remain rejected under 35 U.S.C. 102(b) as being anticipated by US 4,086,363 issued to Cervoni as stated in the office action dated 6/25/08. The rejection has been

modified to reflect the amendments made to the claim and addition of new claim 18. Response to applicant's argument appears at the end of the reiterated rejection.

In the instant invention, applicants claim a method for the treatment of a condition associated with T-cell proliferation or that is mediated by pro- and/or anti-inflammatory cytokines by administering a compound of formula I wherein the compound is selected from bufeniode, denopamine, ifenprodil, isoxsuprine, labetalol, medroxalol, mesuprine, nylidrin, protokylol, ractopamine, ritodrine, salmefamol and sulfinatol.

Cervoni teaches that administration of nylidrin (elected species) to patients for the treatment of asthma and the prevention of asthmatic symptoms (column 1, lines 4-5). The reference discloses that nylidrin is a β-adrenergic stimulator and useful in the treatment of asthma which is a chronic disorder of airway inflammation. The claim 18 as presented recites that the compound is in the form of the enantiomer or diastereomer that has **little** or no activity at an α or β adrenoceptor. Since the nylidrin of Cervoni is a β-adrenergic stimulator it has at least little activity at the β adrenoceptor and hence reads on the instant claim 18. Since nylidrin is administered to patients suffering from asthma, it is inherent that it is treating the disease condition mediated by pro- and/or anti-inflammatory cytokines. This meets the limitations of claims 1 and 18. Hence Cervoni anticipates instant invention.

Response to Arguments

Applicants argue that Cervoni reference does not disclose with certainty the use of nylidrin to treat a condition associated with T-cell proliferation or that is mediated by pro- and/or anti-inflammatory cytokines and hence does not anticipate the instant invention.

Applicant's arguments filed 12/19/08 have been fully considered but they are not persuasive. As stated in the rejection above, in Cervoni, nylidrin (elected species) to patients for the treatment of asthma and the prevention of asthmatic symptoms (column 1, lines 4-5). The reference discloses that nylidrin is a β-adrenergic stimulator and useful in the treatment of asthma which is a chronic disorder of airway inflammation. Since nylidrin is administered to patients suffering from asthma, it is inherent that it is treating the disease condition mediated by pro- and/or anti-inflammatory cytokines.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2 and 18 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,086,363 issued to Cervoni in view of WO 03/092617 of Jost-Price, et al., as stated in the office action dated 6/25/08. The rejection has been modified to reflect the amendments made to the claims 1 and 2, and addition of new claim 18. Response to applicant's argument appears at the end of the reiterated rejection.

In the instant invention, applicants claim a method for the treatment of a condition associated with T-cell proliferation or that is mediated by pro- and/or anti-inflammatory cytokines by administering a compound of formula I wherein the compound is selected from bufeniode, denopamine, ifenprodil, isoxsuprine, labetalol, medroxalol, mesuprine, nylidrin, protokylol, ractopamine, ritodrine, salmefamol and sulfinatol.

Cervoni teaches that administration of nylidrin (elected species) to patients for the treatment of asthma and the prevention of asthmatic symptoms (column 1, lines 4-5). The reference discloses that nylidrin is a β-adrenergic stimulator and useful in the treatment of asthma which is a chronic disorder of airway inflammation. The claim 18 as presented recites that the compound is in the form of the enantiomer or diastereomer that has **little** or no activity at an α or β adrenoceptor. Since the nylidrin of Cervoni is a β-adrenergic stimulator it has at least little activity at the β adrenoceptor and hence reads on the instant claim 18. Since nylidrin is administered to patients suffering from asthma, it is inherent that it is treating the disease condition mediated by pro- and/or anti-inflammatory cytokines. This meets the limitations of claims 1 and 18.

Cervoni does not teach that compounds of formula I used in the treatment of rheumatoid arthritis (elected species) which is a disease associated T-cell proliferation or mediated by pro- and/or anti-inflammatory cytokines.

The reference of Jost-Price discloses combination of β-adrenergic receptor ligand and a steroid (claim 5 of the Jost-Price, page 18). The β-adrenergic receptor ligand selected from labetalol, ritodrine, medroxalol, etc., (claim 6 of the cited reference). The claim 1 of the instant application is drawn with a transitional phrase "comprising" and hence the instant claim as recited does not preclude other agents such as a steroid being present in the method steps of instant claim 1 and 18. Jost-Price also discloses that inflammatory skin disorders occurs in people who have family history of asthma (page 1, line 14) and psoriasis a common chronic proliferative skin disease (page 1, line 22) has some association with arthritis (page 1, line 30). The reference also teaches that TNF-α is a major mediator of inflammation (page 2, line 14). The fact that arthritis is associated with TNF-α, a cytokine reads on the instant claims 1, 2 and 18.

It would have been obvious to one of ordinary skill in the art at the time the invention combine the teachings of Cervoni and Jost-Price to arrive at the instant invention. The skilled artisan would have been motivated to do so given the fact that arthritis is associated to chronic proliferative skin disease such as psoriasis which occurs in people who have a family history of asthma. Josh-Price uses a combination of therapy of β-adrenergic receptor ligand such as ritodrine, labetalol, medroxalol, etc., whose structural features corresponds to formula I of instant invention (including the elected species nylidrin) along with a steroid such as cortisol. The instant claim as presented with the transitional phrase 'comprising' does not preclude other active ingredients such as a steroid being administered in the method. There would have been a

reasonable expectation of success to use a any other compounds such as labetalol, ritodrine, medroxalol disclosed in Jost-Price in place of nylidrin, and vice versa of Cervoni because they all corresponds to the formula I of instant invention and Jost-Price used the afore-mentioned combination of drug to treat inflammatory skin disorders and the skin disorders are associated with arthritis.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

1. Applicants argue that "taken alone or in combination, do not disclose or suggest the applicants' claimed method for treating rheumatoid arthritis, osteoarthritis or osteoporosis". Applicants also cite KSR case law stating that, "mere fact that the purported prior art could have been modified or applied in some manner to yield an applicant's invention does not make the modification or application obvious unless "there was an apparent reason to combine the known elements in the: fashion claimed" by the applicant. KSR International Co. v. Teleflex Inc., 550

U.S.-(2007). Furthermore, an applicant's invention is not "proved obvious merely by demonstrating that each of its elements was, independently, known in the (purported) prior art." Applicants further cite "*In re Hayashibara and Sugimoto*, 188 USPQ 4 (CCPA 1975)". The PTO Board of Appeals had affirmed a § 103 rejection, and the CCPA reversed, stating: Turning to the.., rejection.., for obviousness under 103, we agree with appellants that there is nothing in the reference which would lead those of ordinary skill in the art to employ [the substance] as appellants do in the product of claim 11 (emphasis added by the office). The reference does not teach [the substance] as possessing any of the characteristics or functions upon which appellants' claimed invention depends (emphasis added).state the

2. Applicant's further state that claim 17 has been cancelled to expedite the prosecution.

Applicant's arguments filed 12/19/08 have been fully considered but they are not persuasive. As stated in the rejection above, Cervoni discloses administration of nylidrin (elected species) to patients for the treatment of asthma and the prevention of asthmatic symptoms (column 1, lines 4-5). The reference discloses that nylidrin is a β-adrenergic stimulator and useful in the treatment of asthma which is a chronic disorder of airway inflammation. Jost-Price also discloses that inflammatory skin disorders occurs in people who have family history of asthma (page 1, line 14) and psoriasis a common chronic proliferative skin disease (page 1, line 22) has some association with arthritis (page 1, line 30). Also, Jost-Price discloses the administration of compounds corresponding to formula I (nylidrin is a species of formula I) and hence discloses use of compounds of formula I to treat arthritis. As illustrated in the rejection, the claim as recited does not preclude the presence of additional agents being present in the

method steps being present in the instant invention. With respect to applicant's cited reference to KSR case law, it should be noted the instant rejection is based on specific teaching, suggestion and motivation (TSM test of Graham and John Deere). It should be noted that KSR forecloses the argument that a specific teaching, suggestion and motivation is required to support a finding of obviousness.

With respect to the case law of *Hayashibara and Sugimoto,* it should be noted that the claim 11 of cited case is drawn to a product and not to a method of administration to treat a disease condition as it is in the instant invention. Also, unlike in the case of *Hayashibara and Sugimoto* case wherein the court noted that the characteristics and functions of the product as claimed by the appellants was not apparent in the prior art, in the instant case, Cervoni discloses that nylidrin is administered to treat patients for the treatment of asthma and the prevention of asthmatic symptoms; and nylidrin is a β-adrenergic stimulator and useful in the treatment of asthma that is a chronic disorder of airway inflammation.

2. Applicant's argument that "claim 17 has been canceled in an attempt to advance the prosecution" is not persuasive. Because, the instant claims 1 and 18 as recited, are drawn with the transitional phrase "comprising", and hence the method of administration of a combination of active ingredients as disclosed by Jost-Price is not precluded. Hence the rejection under obviousness is proper and is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). The amendments to claims 1 and 2, and addition of claim 18 does not overcome the rejections of record as presented in the modified form here.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Satyanarayana R Gudibande/
Examiner, Art Unit 1654

/Andrew D Kosar/
Primary Examiner, Art Unit 1654